

for the targeting ligand of the particle. Targeted nanoparticles of this sort have advantages over nanoparticles with a plurality of targeting ligands, such as having a smaller overall size, due to having fewer surface ligands, and have fewer ligands to mediate nonspecific binding through avidity-based interactions, rather than affinity-based interactions. Additionally, nanoparticles that contain or carry a therapeutic agent can be successfully targeted to location of interest (such as a cell or tissue) using only a single targeting ligand, thereby delivering the therapeutic agent to the target at a very high targeting ligand-to-therapeutic ratio. This aspect of the described nanoparticles can significantly increase the efficiency of making such therapeutics while also reducing the need to employ a high number of costly antibodies to mediate targeting.

**[0021]** Nanoparticles herein described and related compositions, methods, and systems can be used in several embodiments as a flexible molecular structure suitable for carrying compounds of various sizes, dimensions and chemical nature.

**[0022]** Nanoparticles herein described and related compositions, methods, and systems can be used in several embodiments as delivery systems which can provide protection of the carried compound from degradation, recognition by immune system and loss due to combination with serum proteins or blood cells.

**[0023]** Nanoparticles herein described and related compositions, methods, and systems can be used in several embodiments as delivery systems characterized by steric stabilization and/or ability to deliver the compound to specific targets such as tissues, specific cell types within a tissue and even specific intracellular locations within certain cell types.

**[0024]** Nanoparticles herein described and related compositions, methods, and systems can be designed in several embodiments, to release a carried compound in a controllable way, including controlled release of multiple compounds within a same nanoparticle at different rates and/or times.

**[0025]** Nanoparticles herein described and related compositions, methods, and systems can be used in several embodiments, to deliver compounds with enhanced specificity and/or selectivity during targeting and/or enhanced recognition of the compound by the target compared to certain systems of the art.

**[0026]** Nanoparticles herein described and related compositions, methods, and systems can be used in several embodiments in connection with applications wherein controlled delivery of a compound of interest is desirable, including but not limited to medical applications, such as therapeutics, diagnostics and clinical applications. Additional applications comprise biological analysis, veterinary applications, and delivery of compounds of interest in organisms other than animals, and in particular in plants.

**[0027]** The details of one or more embodiments of the disclosure are set forth in the accompanying drawings and the detailed description and examples below. Other features, objects, and advantages will be apparent from the detailed description, examples and drawings, and from the appended claims

one or more embodiments of the present disclosure and, together with the detailed description and the examples, serve to explain the principles and implementations of the disclosure.

**[0029]** FIG. 1 shows a schematic representation of a nanoparticle and a related method for the relevant formation in absence of a boronic acid containing compound. Panel A shows a schematic representation of a polymer containing a polyol (MAP, 4) and a compound of interest (nucleic acid) according to an embodiment herein described. Panel B shows a nanoparticle formed upon assembly of the polymer containing a polyol and compound shown in panel A.

**[0030]** FIG. 2 shows a schematic representation of a nanoparticle and a related method of manufacturing according to an embodiment of the present disclosure. Panel A shows a polymer containing a polyol (MAP, 4) and a polymer containing a boronic acid (BA-PEG, 6) together with a molecule of interest (nucleic acid) according to an embodiment of the present disclosure. Panel B shows a BA-pegylated stabilized nanoparticle formed upon assembly of the polymers and compound shown in panel A.

**[0031]** FIG. 3 shows formation of a complex comprising polymers containing polyols and a compound of interest according to an embodiment herein described. In particular, FIG. 3, shows results of a MAP gel retardation assay with plasmid DNA according to an embodiment of the present disclosure. A DNA ladder is loaded in Lane 1. Lanes 2-8 show plasmid DNA combined with MAP of incrementally increased charge ratio. Charge ratio is defined as the amount of positive charges on the MAP divided by the amount of negative charges on the nucleic acid.

**[0032]** FIG. 4 shows formation of a complex comprising polymers containing polyols and a compound of interest according to an embodiment herein described. In particular, FIG. 4 shows results of a MAP gel retardation assay with siRNA according to an embodiment of the present disclosure. A DNA ladder is loaded in Lane 1. Lanes 2-8 show siRNA combined with MAP of incrementally increased charge ratio.

**[0033]** FIG. 5 shows properties of nanoparticles according to some embodiments herein described. In particular, FIG. 5 shows a diagram illustrating a plot of particle size (determined from dynamic light scattering (DLS) measurements) versus charge ratio and zeta potential (a property that relates to the surface charge of the nanoparticle) versus charge ratio for MAP-plasmid nanoparticles according to an embodiment of the present disclosure.

**[0034]** FIG. 6 properties of nanoparticles according to some embodiments herein described. In particular, FIG. 6 shows a diagram illustrating a plot of particle size (DLS) versus charge ratio and zeta potential versus charge ratio for BA-PEGylated MAP-plasmid nanoparticles according to an embodiment of the present disclosure.

**[0035]** FIG. 7 shows the salt stability of BA-PEGylated MAP-Plasmid Nanoparticles according to an embodiment herein disclosed. Plot A: 5:1 BA-PEG+np+1xPBS after 5 mins; Plot B: 5:1 BA-PEG+np, dialyzed 3x w/100 kDa+1xPBS after 5 mins; Plot C: 5:1 prePEGylated w/BA-PEG+1xPBS after 5 mins; Plot D: 5:1 prePEGylated w/BA-PEG, dialyze 3x w/100 kDa+PBS after 5 mins.

**[0036]** FIG. 8 shows delivery of an agent to human cells in vitro with nanoparticles according to an embodiment herein described. In particular, FIG. 8 shows a diagram illustrating a plot of relative light units (RLU) that are a

#### BRIEF DESCRIPTION OF THE DRAWINGS

**[0028]** The accompanying drawings, which are incorporated into and constitute a part of this specification, illustrate